Good morning. Vaccinations have begun!

Today under COVD-19 News I provide the ACOG guidance on vaccination, the updated NIH Treatment Guidelines on baricitinib plus remdesivir, the initial review on the Moderna vaccine, the WHO update on masking, and the FDA authorizing the first fully at-home, over the counter COVID-19 antigen test. Under Journal Reviews an article on GBS and COVID-19, an evaluation of cloth masks and modified procedure masks as PPE, the prepublication result on azithromycin and COVID-19 from the RECOVERT Trial, and the impact of immunization during the pandemic in Colorado.

Have a great day-get vaccinated!

Ed

COVID-19 News

Vaccinating Pregnant and Lactating Patients Against COVID-19
ACOG Practice Advisory December 2020
The American College of Obstetricians and Gynecologists has offered guidance on vaccinating pregnant and lactating women with the Pfizer-BioNTech COVID-19 vaccine. Pregnant women were not included in clinical trials leading up to the vaccine's authorization. The group notes that women should not be required to undergo pregnancy tests before receiving the vaccine. They say that vaccines should not be withheld from pregnant women who are eligible for vaccination based on priority groups outlined by the Advisory Committee on Immunization Practices. In addition, vaccination should be offered to lactating women based on their priority group.

The COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of Baricitinib for the Treatment of COVID-19
December 14, 2020
The National Institutes of Health's COVID-19 Treatment Guidelines Panel says that there is currently not enough evidence to recommend for or against use of baricitinib plus remdesivir in COVID-19 inpatients when corticosteroids are an option. When corticosteroids cannot be given, the panel recommends baricitinib plus remdesivir in nonintubated inpatients requiring supplemental oxygen. Baricitinib should not be given as a monotherapy, and it should not be coadministered with corticosteroids.

Initial Moderna Submission
The FDA's reviewed the 30,000-person clinical study confirming Moderna's earlier disclosure that the vaccine was 94.1% effective at preventing Covid-19 disease with symptoms, including severe disease. The agency also said there were no specific safety concerns that would preclude authorization. Moderna's analysis also included new data suggesting that the first dose of its vaccine can reduce asymptomatic infections. If this finding holds up in further analysis—including after the second of the two-dose regimen—it could mean that the vaccine not only protects individuals from disease, but also curbs transmission of the virus from person to person. Pfizer is also studying this as well and should report out early next year. If the vaccines demonstrate that they reduce transmission as well this would be a big deal. A vaccine that prevents asymptomatic infections and curbs viral transmission could hasten the end of the coronavirus pandemic if enough people get vaccinated. The FDA analysis found the Moderna vaccine appeared somewhat more effective in younger people than in seniors. Vaccine efficacy was 95.6% among people 18 to 64, and 86.4% among those 65 and older. Moderna studied its vaccine in

people 18 and older and is seeking authorization for use in that population. Pfizer approval is for people 16 and older. The most common adverse reactions included pain at the injection site, fatigue, headache, muscle pain, joint pain, and chills; these were usually short-lived. Three vaccine recipients and one placebo recipient developed Bell's palsy. The FDA says, "Causality assessment is confounded by predisposing factors in these participants. However, a potential contribution of the vaccine to the manifestations of these events of facial palsy cannot be ruled out." The agency plans to recommend ongoing monitoring for Bell's once widespread vaccination begins.

WHO Updated Guidelines on Masks
December 9, 2020
WHO tightened guidelines on wearing face masks, recommending that, where COVID-19 is spreading, they be worn by everyone in health care facilities and for all interactions in poorly-ventilated indoor spaces. The WHO also said that, where the pandemic was spreading, people - including children and students aged 12 or over [I would argue children over age 2 can safely wear masks] - should always wear masks in shops, workplaces, and schools that lack adequate ventilation, and when receiving visitors at home in poorly ventilated rooms. Masks should also be worn outdoors and in well ventilated indoor spaces where physical distancing of at least one meter (3 ft) could not be maintained. In areas of COVID-19 spread, it also advised "universal" wearing of medical masks in health care facilities, including when caring for other patients. Health care workers could wear N95 respirator masks if available when caring for COVID-19 patients, but their only proven protection is when they are doing aerosol-generating procedures which carry higher risks, the WHO said.

It recommended that people doing vigorous physical activity not wear masks, citing some associated risks, particularly for people with asthma. [most people can safely wear masks for most exercising] Adequate ventilation, physical distancing and disinfection of "high-touch surfaces" in the gym must be maintained, or their temporary closure should be considered.

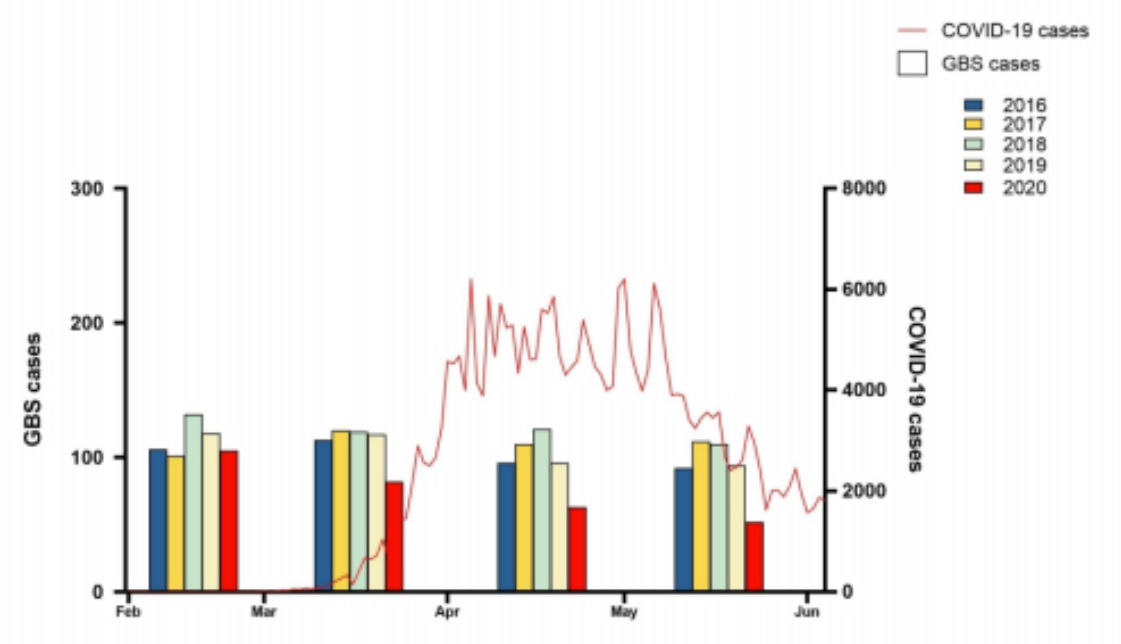
Coronavirus (COVID-19) Update: FDA Authorizes Antigen Test as First Over-the-Counter Fully At-Home Diagnostic Test for COVID-19
December 15, 2020
The FDA on Tuesday authorized the first fully at-home, over the counter COVID-19 antigen test. The Ellume COVID-19 Home Test provides results in about 20 minutes. It is authorized for use in people ages 2 years and up. For people with symptoms, the test accurately identified 96% of positive samples and 100% of negative samples. Among those without symptoms, the test identified 91% of positive samples and 96% of negative ones. This is a rapid, lateral flow antigen test, a type of test that runs a liquid sample along a surface with reactive molecules. The test detects fragments of proteins of the SARS-CoV-2 virus from a nasal swab sample. Like other antigen tests, a small percentage of positive and negative results from this test may be false. Therefore, for patients without symptoms, positive results should be treated as presumptively positive until confirmed by another test as soon as possible. This is especially true if there are fewer infections in a particular community, as false positive results can be more common when antigen tests are used in populations where there is little COVID-19 (low prevalence). A Bluetooth-connected analyzer for use with an app on the user's smartphone is provided. The sample is analyzed, and results are automatically transmitted to the user's smartphone.

Journal Reviews

Epidemiological and Cohort Study Finds No Association Between COVID-19 and Guillain-Barré Syndrome

Brain published online
https://doi.org/10.1093/brain/awaa433

This epidemiological and cohort study sought to investigate any causative association between COVID-19 infection and GBS. The epidemiology of GBS cases reported to the UK National Immunoglobulin Database was studied from 2016 to 2019 and compared to cases reported during the COVID-19 pandemic. Data were stratified by hospital trust and region, with numbers of reported cases per month. In parallel, but separately, members of the British Peripheral Nerve Society prospectively reported incident cases of GBS during the pandemic at their hospitals to a central register. The clinical features, investigation findings and outcomes of COVID-19 (definite or probable) and non-COVID-19 associated GBS cases in his cohort were compared. The incidence of GBS treated in UK hospitals from 2016 to 2019 was 1.65–1.88 per 100 000 individuals per year. GBS incidence fell between March and May 2020 compared to the same months of 2016–19. In an independent cohort study, 47 GBS cases were reported (COVID-19 status: 13 definite, 12 probable, 22 non-COVID-19). There were no significant differences in the pattern of weakness, time to nadir, neurophysiology, CSF findings or outcome between these groups. Intubation was more frequent in the COVID-19 affected cohort (7/13, 54% versus 5/22, 23% in COVID-19-negative) likely related to COVID-19 pulmonary involvement.



Comment: Although it is not possible to absolutely rule out the possibility of a link this study finds no epidemiological or phenotypic clues of SARS-CoV-2 being causative of GBS. GBS incidence actually fell during the pandemic, which may be the influence of lockdown measures reducing transmission of GBS inducing pathogens such as Campylobacter jejuni and respiratory viruses. The investigators also studied the protein structure of SARS-CoV-2 to determine whether it—like *Campylobacter*—has human-like antigens that could cause an autoimmune response leading to GBS. Their analysis shows SARS-CoV-2 contains no additional immunogenic material known or proven to drive GBS. Concerns that a COVID vaccination might cause GBS appear very unlikely.

Evaluation of Cloth Masks and Modified Procedure Masks as Personal Protective Equipment for the Public During the COVID-19 Pandemic

JAMA Intern Med published online December 10, 2020
doi:10.1001/jamainternmed.2020.8168

In this publication studies showed that some masks were as much as 79 percent effective at blocking particles that could carry the virus. These were masks made of two layers of woven nylon and fit snug against the wearer's face. Unmodified medical procedure masks with ear loops - also known as surgical masks - offered 38.5 percent filtration efficacy, but when the ear loops were tied in a specific way to tighten the fit, the efficacy improved to 60.3 percent. And when a layer of nylon was added, these masks offered 80 percent effectiveness.

Modifications to surgical masks can enhance the filtering capabilities and reduce inhalation of airborne particles by improving the fit of the mask. They demonstrated that the fitted filtration efficiencies of many consumer-grade masks were nearly equivalent to or better than surgical masks.

As the adoption of face coverings during the COVID-19 pandemic became commonplace, there was a rapid expansion in the public use of commercial, home-made, and improvised masks which vary considerably in design, material, and construction. There have been a number of innovative devices, and mask enhancements that claim to improve the performance characteristics of conventional masks - typically surgical or procedure masks. Despite their widespread dissemination and use during the pandemic, there have been few evaluations of the efficiency of these face coverings or mask enhancements at filtering airborne particles.

In this study, the researchers used a recently described methodological approach based on the OSHA Fit Test to determine the fitted filtration efficiency (FFE) of a variety of consumer-grade and improvised facemasks, as well as several popular modifications of medical procedure masks. Seven consumer-grade masks and five medical procedure mask modifications were fitted on an adult male, and FFE measurements were collected during a series of repeated movements of the torso, head, and facial muscles as outlined by the OSHA Quantitative Fit Testing Protocol.

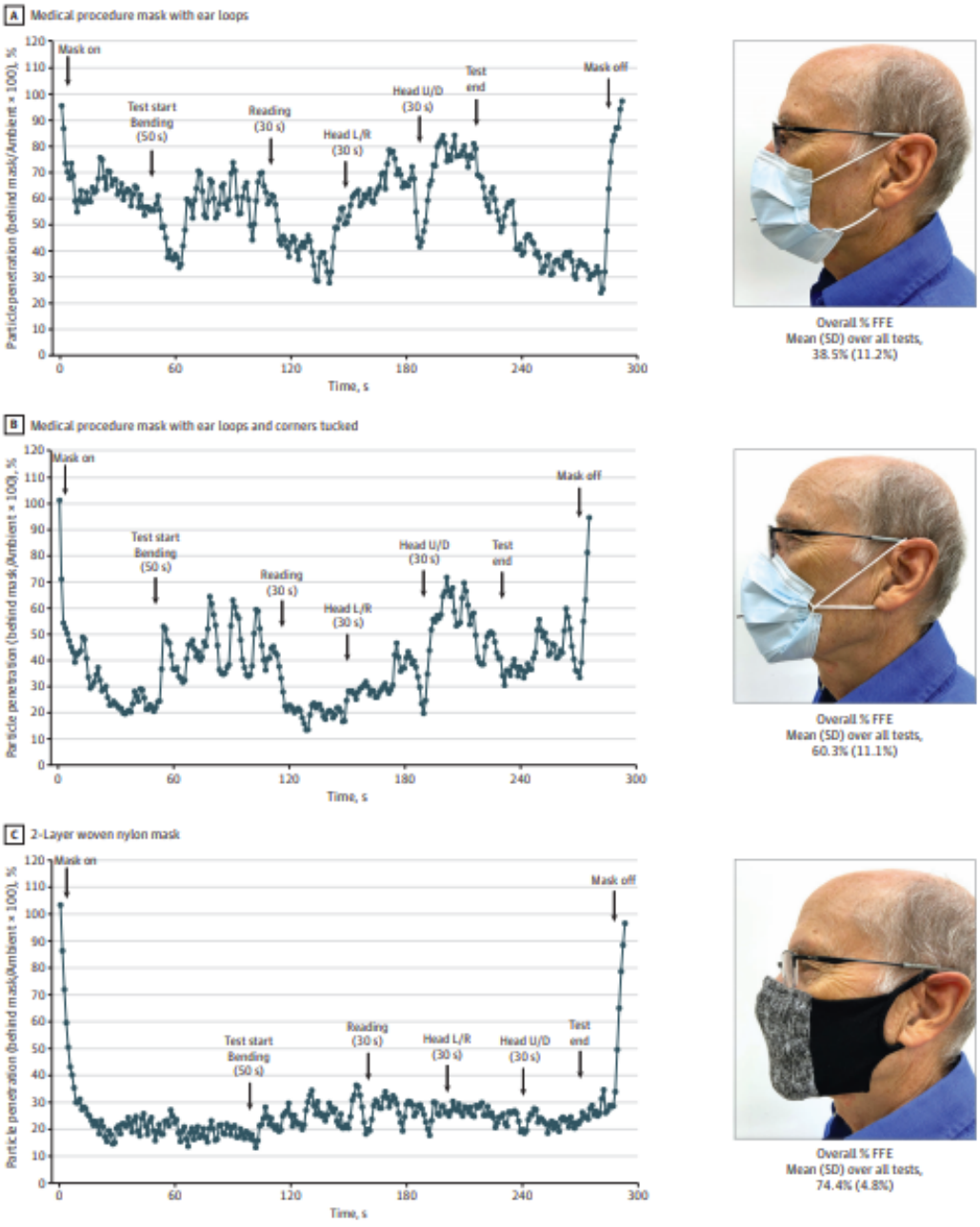
Here are the different mask types with filtration efficacy

Consumer-grade facemasks:

2-layer woven nylon mask, ear loops, w/o aluminum nose bridge: 44.7%
2-layer woven nylon mask, ear loops, w/ aluminum nose bridge: 56.7%
2-layer woven nylon mask, ear loops, w/ nose bridge, 1 non-woven insert: 74.4%
2-later woven nylon mask, ear loops, w/ nose bridge, washed, no insert: 79%
Cotton bandana - folded Surgeon General style: 50%
Cotton bandana - folded "Bandit" style: 49 %
Single-layer woven polyester gaiter/neck cover (balaclava bandana): 37.8%
Single-layer woven polyester/nylon mask with ties: 39.7%
Non-woven polypropylene mask with fixed ear loops: 28.6%
Three-layer woven cotton mask with ear loops: 26.5%

Medical facemasks and modifications:

3M 9210 NIOSH-approved N95 Respirator: 98%
Surgical mask with ties: 71.4%
Procedure mask with ear loops: 38.5%
Procedure mask with ear loops + "loops tied and corners tucked in": 60.3%
Procedure mask with ear loops + "Ear Guard": 61.7%
Procedure mask with ear loops + "23mm claw hair clip": 64.8%
Procedure mask with ear loops + "Fix-the Mask (3 rubber bands)": 78.2%
Procedure mask with ear loops + "nylon hosiery sleeve": 80.2%



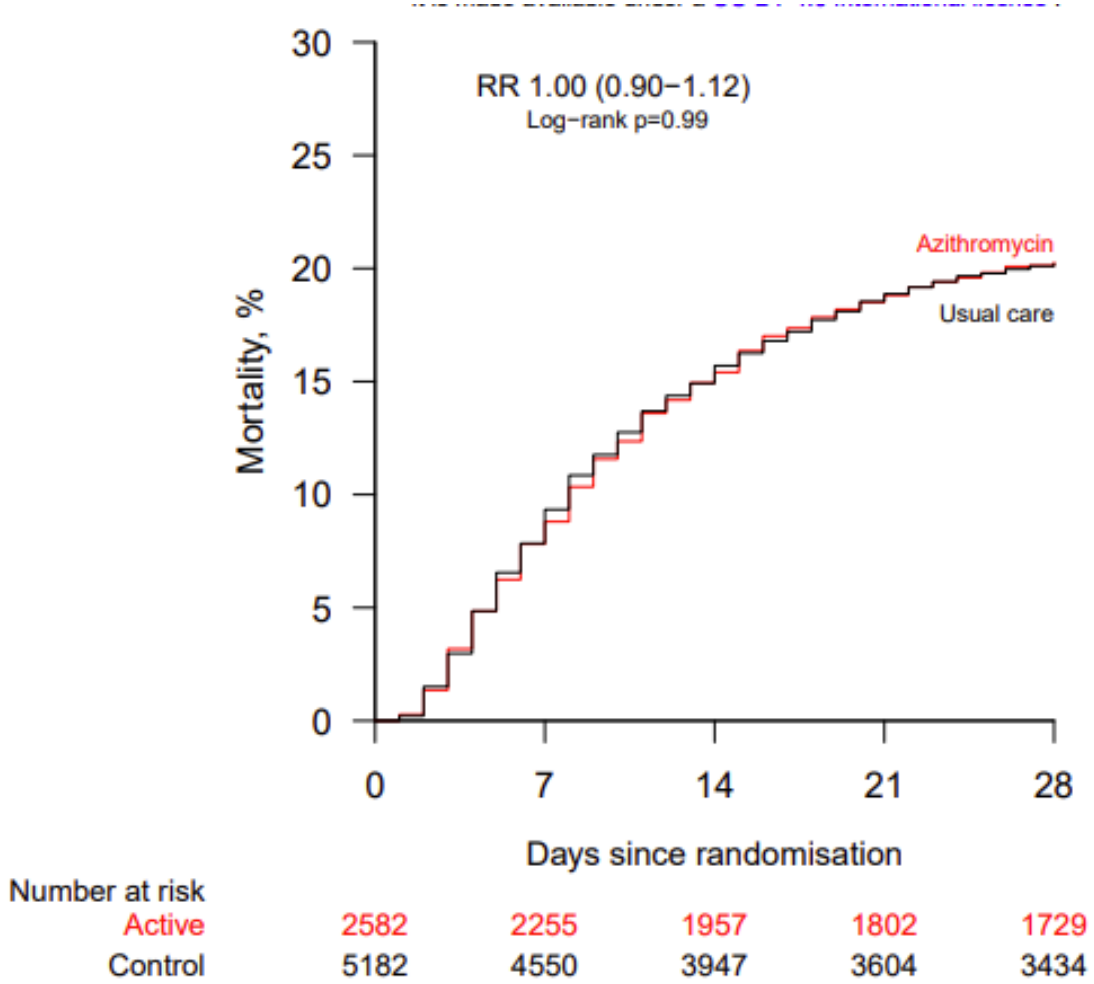
Comment: The key finding in this study is that modifications to surgical masks to improve the fit of the mask can enhance the filtering capabilities and reduce inhalation of airborne particles. They also found that the fitted filtration efficiencies of many consumer-grade masks were nearly equivalent to or better than surgical masks.

Azithromycin in Hospitalised Patients with COVID-19 (RECOVERY): A Randomised, Controlled, Open-Label, Platform Trial

medRxiv posted December 14, 2020

Azithromycin has been proposed as a treatment for COVID-19 based on its immunomodulatory actions and potential antiviral along with HDQ. The investigators evaluated the efficacy and safety of azithromycin in hospitalized patients with COVID-19. This was another randomized, controlled, open-label, adaptive platform trial, several possible treatments were compared with usual care in patients hospitalized with COVID-19 in the UK. (RECOVERY) Eligible and consenting patients were randomly allocated to either usual standard of care alone or usual standard of care plus azithromycin 500 mg once daily by mouth or intravenously for 10 days or until discharge. Patients were twice as likely to be randomized to usual care as to any of the active treatment groups. The primary outcome was 28-day mortality.

Between 7 April and 27 November 2020, 2582 patients were randomly allocated to receive azithromycin and 5182 patients to receive usual care alone. Overall, 496 (19%) patients allocated to azithromycin and 997 (19%) patients allocated to usual care died within 28 days. Consistent results were seen in all pre-specified subgroups of patients. There was no difference in duration of hospitalization (median 12 days vs. 13 days) or the proportion of patients discharged from hospital alive within 28 days (60% vs. 59%; rate ratio 1.03; 95% CI 0.97-1.10; p=0.29). Among those not on invasive mechanical ventilation at baseline, there was no difference in the proportion meeting the composite endpoint of invasive mechanical ventilation or death (21% vs. 22%; risk ratio 0.97; 95% CI 0.89-1.07; p=0.54).



Comment: In patients hospitalized with COVID-19, azithromycin did not provide any clinical benefit. Azithromycin use in patients hospitalized with COVID-19 should be restricted to patients where there is a clear antimicrobial indication. Prior RCTs found that allocation of hospitalized patients with COVID-19 to azithromycin and hydroxychloroquine, was not associated with any improvement in mortality, duration of hospital stay, or clinical status as assessed using an ordinal outcome scale. The findings in this study do not address the use of macrolides for the treatment of non-hospitalized COVID-19 patients with early, mild disease, the results do show that azithromycin is not an effective treatment for hospitalized COVID-19 patients. Bottom line, HDQ and AZ do NOT work and may be associated with serious side effects. This paper is currently undergoing peer review.

Number of Childhood and Adolescent Vaccinations Administered Before and After the COVID-19 Outbreak in Colorado

JAMA Pediatrics published online December 7, 2020

doi:10.1001/jamapediatrics.2020.4733

Data were pulled from the Colorado Immunization Information System. Approximately 87.5% of known immunizing health care professionals report to the Colorado Immunization Information System. All children younger than 6 years have an immunization record in the system, and 85.2% of vaccinations administered in 2019 to individuals aged 0 to 18 years were reported to the Colorado Immunization Information System within the same day. Using data from January 5, 2020, to May 2, 2020, an

interrupted time series analysis was used to measure the association of COVID-19 with immunizations administered. Three age categories were reported (0-2 years, 3-9 years, and 10-17 years) to reflect the recommended US childhood vaccination schedule.

All age groups had a significant drop in immunizations immediately following social distance guidance release (March 15, 2020). In individuals aged 0 to 2 years, the rate of immunizations dropped by 4581 (95% CI, 2965-6196) immunizations per week (P<.001). In individuals aged 3 to 9 years, it dropped by 2486 (95% CI, 568-4408) immunizations per week (P > .99), and in individuals aged 10 to 17 years, it dropped by 4060 (95% CI, 2156-5965) immunizations per week (P<.001).

Figure 1. Interrupted Time Series Analysis for Total Vaccine Doses Administered, January 5 Through May 2, 2020, by Age Group

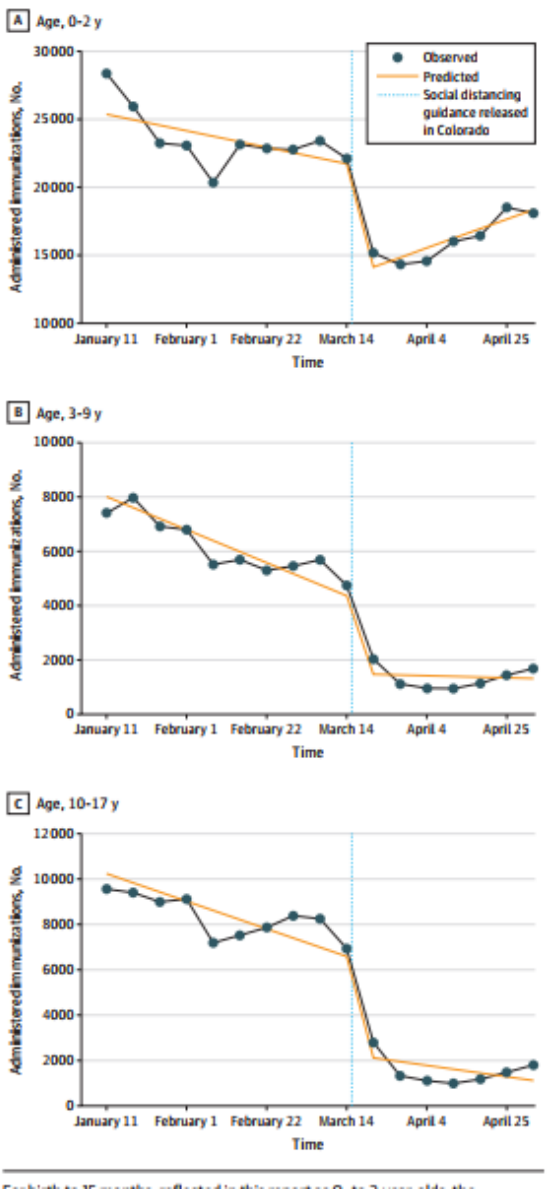
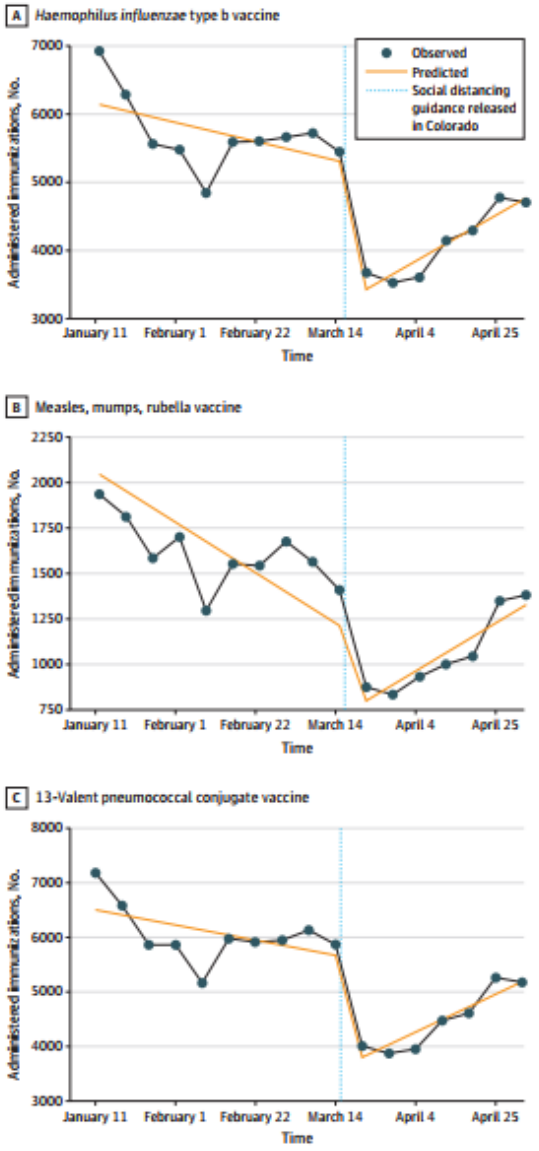


Figure 2. Interrupted Time Series Analysis for Specific Vaccine Doses Administered, January 5 Through May 2, 2020, for Individuals Aged 0 to 2 Years



Comment: Since the onset of the COVID-19 pandemic, vaccination uptake in children and adolescents has shown a significant decrease in Colorado and elsewhere. The clinical implications of this report and

others raises the potential for increasing vaccine-preventable diseases. This is yet another unintended consequence of the pandemic.